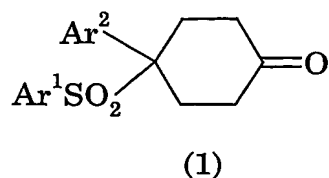


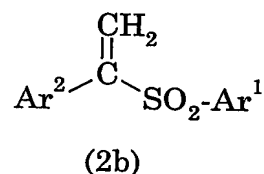
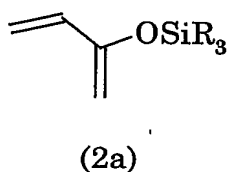
CLAIMS

1. A method of preparing a cyclohexanone of formula (1):

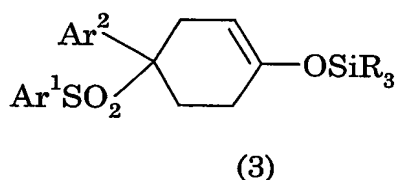


5 comprising:

- (a) cycloaddition of a 2-trialkylsilyloxybutadiene of formula (2a) to a vinyl derivative of formula (2b):



to form a silyl enol ether of formula (3):



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and

- (b) hydrolysis of said silyl enol ether to form the cyclohexanone of formula (1);

wherein, in formulae (1), (2a), (2b) and (3), R represents C<sub>1-6</sub> alkyl;

15 Ar<sup>1</sup> represents C<sub>6-10</sub>aryl or heteroaryl, either of which bears 0-3 substituents independently selected from halogen, CN, NO<sub>2</sub>, CF<sub>3</sub>, OH, OCF<sub>3</sub>, C<sub>1-4</sub>alkoxy or C<sub>1-4</sub>alkyl which optionally bears a substituent selected from halogen, CN, NO<sub>2</sub>, CF<sub>3</sub>, OH and C<sub>1-4</sub>alkoxy; and

20 Ar<sup>2</sup> represents C<sub>6-10</sub>aryl or heteroaryl, either of which bears 0-3 substituents independently selected from halogen, CN, NO<sub>2</sub>, CF<sub>3</sub>, OH, OCF<sub>3</sub>, C<sub>1-4</sub>alkoxy or C<sub>1-4</sub>alkyl which optionally bears a substituent selected from halogen, CN, NO<sub>2</sub>, CF<sub>3</sub>, OH and C<sub>1-4</sub>alkoxy.

2. A method according to claim 1 wherein the cycloaddition reaction between the vinyl derivative (2b) and 2-trialkylsilyloxybutadiene (2a) to form silyl enol ether (3) is carried out at 100-150°C in a hydrocarbon solvent under an inert atmosphere.

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3. A method according to claim 1 or claim 2 wherein hydrolysis of the silyl enol ether (3) to the cyclohexanone (1) is carried out *in situ* without isolation or further purification of the silyl enol ether.

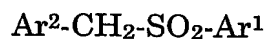
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4. A method according to claim 3 wherein said hydrolysis is carried out by treatment with aqueous mineral acid at 30-80°C.

5. A method according to any previous claim wherein each R represents methyl.

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6. A method according to any previous claim wherein the vinyl derivative (2) is prepared by reaction of a sulphone (4):



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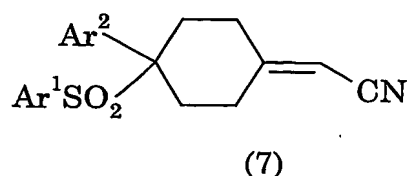
(4)

with N,N,N',N'-tetramethyldiaminomethane and acetic anhydride in DMF and Ar<sup>1</sup> and Ar<sup>2</sup> are as defined in claim 1.

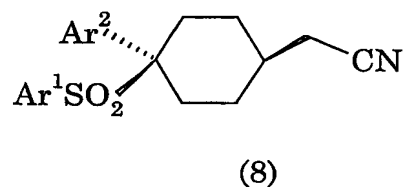
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7. A method according to any previous claim comprising the additional steps of:

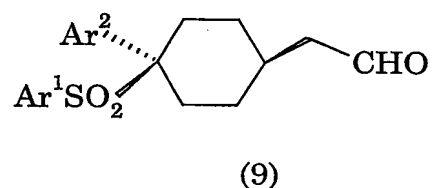
(c) reacting a cyclohexanone of formula (1) with a di(C<sub>1-4</sub>alkyl) cyanomethylphosphonate and base to form a cyclohexylideneacetonitrile (7):



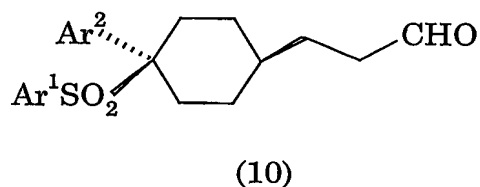
(d) reducing said cyclohexylideneacetonitrile with lithium tri-*sec*-butylborohydride to form the corresponding *cis* cyclohexaneacetonitrile (8):



5 (e) sequential treatment of said *cis* cyclohexaneacetonitrile with diisobutylaluminium hydride and aqueous acid to form the corresponding *cis* cyclohexaneacetaldehyde (9):



10 (f) homologation of said *cis* cyclohexaneacetaldehyde to the corresponding *cis* cyclohexanepropanal (10):



and

(g) oxidising said *cis* cyclohexanepropanal to the corresponding *cis* cyclohexanepropanoic acid (6);

15 wherein Ar¹ and Ar² are as defined in claim 1 and “*cis*” refers to the stereoconfiguration of the side chain relative to the Ar¹SO₂ group.

20 8. A method according to claim 7 wherein in step (c) the C<sub>1-4</sub> alkyl groups are ethyl, the reaction is carried out in THF at 0°C or below and the base is potassium *t*-butoxide.

9. A method according to claim 7 or claim 8 wherein the reduction in step (d) is carried out in THF at about -60°C.

5 10. A method according to any of claims 7 to 9 wherein the homologation in step (f) is effected by reaction of the *cis* cyclohexaneacetaldehyde (9) with a methoxymethyltriphenylphosphonium salt and strong base, followed by hydrolysis of the resulting mixture of enol ethers with aqueous acid.

10 11. A method according to any of claims 7 to 10 comprising the additional step of neutralising the cyclohexanepropanoic acid (6) with sodium hydroxide to form the sodium salt thereof.

15 12. A method according to any previous claim wherein Ar<sup>1</sup> represents 4-chlorophenyl, 4-trifluoromethylphenyl or 6-trifluoromethylpyridin-3-yl and Ar<sup>2</sup> represents 2,5-difluorophenyl or 2,3,6-trifluorophenyl.

20 13. A method of preparing sodium *cis*-4-[(4-chlorophenyl)sulfonyl]-4-(2,5-difluorophenyl)cyclohexanepropanoate comprising the steps of:

(i) preparing 4-[(4-chlorophenyl)sulfonyl]-4-(2,5-difluorophenyl)cyclohexanone by the method of claim 1 wherein Ar<sup>1</sup> represents 4-chlorophenyl and Ar<sup>2</sup> represents 2,5-difluorophenyl;

25 (ii) reacting the product of step (i) with diethyl cyanomethylphosphonate and potassium *tert*-butoxide to form [4-[(4-chlorophenyl)sulfonyl]-4-(2,5-difluorophenyl)cyclohexylidene]-acetonitrile;

30 (iii) reducing the product of step (ii) with lithium tri-*sec*-butylborohydride to form *cis*-4-[(4-chlorophenyl)sulfonyl]-4-(2,5-difluorophenyl)cyclohexaneacetonitrile;

(iv) reacting the product of step (iii) sequentially with diisobutylaluminium hydride and with aqueous acid to form *cis*-4-[(4-chlorophenyl)sulfonyl]-4-(2,5-difluorophenyl)cyclohexanepropanal;

5 (v) reacting the product of step (iv) with methoxymethyltriphenylphosphonium chloride and potassium *tert*-butoxide, then hydrolysing the resulting mixture of enol ethers with aqueous acid to form *cis*-4-[(4-chlorophenyl)sulfonyl]-4-(2,5-difluorophenyl)cyclohexanepropanal;

(vi) oxidising the product of step (v) with aqueous sodium chlorite and sulphamic acid to form *cis*-4-[(4-chlorophenyl)sulfonyl]-4-(2,5-difluorophenyl)cyclohexanepropanoic acid; and  
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(vii) neutralising the product of step (vi) with sodium hydroxide.